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PATENT
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Appellants	:	Powell et al.
Serial No.	:	09/303,716
Filed	:	April 30, 1999
For	:	TRANSITION STATE ANALOGS
Group Art Unit	:	1652
Examiner	:	C.L. Patterson, Jr.

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents Washington, D.C. 20231, on August 20, 2002

Gerard Bilotto, Reg. No. P-51,474
Name of Appellant, Assignee or Registered Representative

Signature

August 20, 2002
Date of Signature

REPLY BRIEF

Commissioner for Patents
Washington, D.C., 20231

Sir:

Appellants submit herewith a Reply Brief under provisions 37 C.F.R. 1.193(b)(1). In response to the Examiner's Answer, mailed June 20, 2002, (the "Examiner's Answer"). Appellants respectfully request that the Reply Brief be considered and entered in the record. Although not specifically required by the Patent Rules the Reply Brief is hereby submitted in triplicate as a courtesy to the Board.

No fee is believed due for entry and consideration of this Reply Brief. However, the Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account **No. 50-0540**.

ARGUMENT

A. Response to paragraph (3) ("*Status of Claims*") of the Examiner's Answer.

Appellants thank the Examiner for correcting the status of claims.

B. Response to paragraph (10) ("*Grounds of Rejection*") of the Examiner's Answer:

The Examiner maintains the rejection of claims 36, 39, 42, 45 and 48 under the "written description" requirement of 35 U.S.C. § 112, first paragraph and specifically states that " the instant rejection is not an enablement rejection" (Examiner's Answer, par. 11, page 7, emphasis in the original). Therefore, Appellants will only address the compliance of the claims to the "written description" requirement. Appellants refer to the Appeal Brief, dated April 30, 2002, (the "Appeal Brief") for arguments regarding the enablement requirement of 35 USC § 112, first paragraph (Appeal Brief, pages 8-16).

Appellants respectfully direct the Examiner's attention to MPEP §§2163-2163.07 which sets forth the standard for determining whether an applicant has satisfied the "written description" requirement of 35 USC § 112, first paragraph. One of ordinary skill in the art would readily recognize from the disclosure in the Specification that Appellants invented the claimed subject matter. The function of the written description requirement is to ensure that a patent is granted to inventors who had possession, as of the filing date of the application relied on, of the specific subject matter later

claimed by them; **how the Specification accomplishes this is not material**. *In re Smith*, 178 U.S.P.Q. 620 (CCPA 1973). [See also, MPEP, Section 2163.02].

> [T]he 'essential goal' of the description of the invention requirement is to clearly convey the information that an applicant has invented the subject matter which is claimed.

In re Barker, 194 USPQ 470 (CCPA 1977). (See, MPEP 2163).

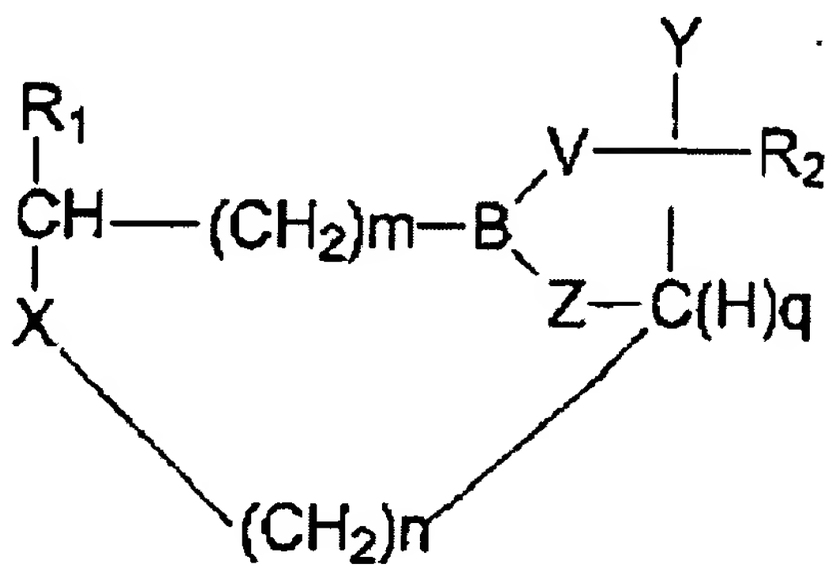
Pursuant to the "written description" requirement of 35 U.S.C. § 112, first paragraph each claim limitation finds support in the Specification and there is no basis for the Examiner's objection. Appellants' claims are "literally" supported by the disclosure. Accordingly, the rejection is improper and should be reversed.

Appellants further direct the Examiner's attention to the USPTO Revised Interim Written Description Guidelines Training Materials (See, http://www.uspto.gov/web/menu/written.pdf). Appellants submit that Example 16 of the Guidelines (entitled "*Antibodies*") is analogous to the current application as it describes a claim to "An isolated antibody capable of binding to antigen X", where the Specification provides a clear protocol by which antigen X was isolated and describes antibodies which specifically bind to antigen X, but does not disclose specific examples of such antibodies. The Guidelines state that the hypothetical in Example 16 provides an adequate written description of the claimed invention and therefore meets the requirement of 35 USC § 112, first paragraph.

Similarly, the instant Specification describes a method which comprises exposing cells capable of producing antibodies to the antigens comprising the hapten of formula I and thereby generating antibody producing cell. The antibody producing cells are then hybridized with myeloma cells which generate a plurality of hybridoma cells each producing monoclonal antibodies. Methods of screening the plurality of monoclonal antibodies to identify a monoclonal antibody which catalyzes the chemical reaction of interest are also described in the Specification (Prophetic Example 6). A similar analysis applies to each of the presently pending claims and all claim limitations.

Referring to pending claim 36, as an example, Appellants will demonstrate that the currently pending claims are fully supported by the Specification in compliance with the "written description" requirement of 35 U.S.C. § 112, first paragraph.

Claim 36. A catalytic antibody elicited by an antigen comprising the boron-containing hapten of formula I:



(I)

wherein (additional formula limitations omitted).

Appellants submit that claim 36 is fully supported by the Specification which provides an extensive disclosure of the compound of formula (I) (from the bottom of page 25 to the middle of page 26 and page 45, lines 5-24). The above hapten formula (I) is labeled as formula (II) in the original Specification. As discussed in the Appeal Brief, page 3-4, the above hapten formula was re-labeled in the Preliminary Amendment filed April 30, 1999, pages 2-3 from formula (II) to (I). All subsequent page references to the original Specification will refer to the above hapten formula of claim 36.

A detailed description of the various synthetic methods for preparing the compounds of formula (I) are disclosed on page 52, lines 16-22 of the Specification. An extensive disclosure of how to produce the claimed catalytic antibody is provided in the Specification starting on page 56, line 5 to page 61, line 2.

In fact, the Examiner admits that the written description of the haptens of formula (I) satisfies the requirements of 35 U.S.C. § 112, first paragraph. The Examiner states the following:

> The examiner admits that a method of making the hapten is given and claims drawn to this hapten were allowed in the parent application...

[Examiner's Answer, par. 11, page 4].

Instead, the Examiner alleges that "... [the hapten] formula has a very wide range of possibilities; a method for producing a catalytic antibody which catalyzes any chemical reaction 'of interest' by using the hapten of formula (I)..." (Examiner's Answer, par. 10, page 3, emphasis in the original).

Even if the Examiner's allegation were true, which they are not, they would not support a written description rejection. The fact that the claims are broad does not support a "written description" rejection if the claims are otherwise supported by the disclosure.

Moreover, the Examiner's assertion misrepresents the currently pending claims. The hapten of formula I has a tri-substituted boron which acts as a transition-state analog of a peptide or ester bond. The transition-state analog defines a site on a substrate susceptible to the catalysis, whereas the rest of the hapten is used to modulate catalytic antibody specificity. Appellants submit that formula (I) does not describe "a very wide range of possibilities", but rather a narrow class of compounds. The methods of making and using the class of compounds to make the claimed catalytic antibodies are fully within the purview of one of ordinary skill in the art (e.g., a skilled organic synthetic chemist) in view of the teachings and guidance in the present application and what is known in the art.

Furthermore, Appellants submit that the claims of the instant invention are not directed to "a method for producing a catalytic antibody which catalyzes **any** chemical reaction", as asserted by the Examiner. Instead, the chemical reaction to be catalyzed by the antibody is intrinsically determined and defined by the hapten used in the production of the claimed catalytic antibody. In this case, it is determined by a boron-containing hapten of formula (I), which is clearly specified in the currently pending claims of the instant invention. The Specification clearly states:

> The invention is broadly directed to antigens capable of eliciting through immunogenic methods **catalytic antibodies which can catalyze the cleavage or formation of a peptide linkage or an ester bond** in a molecule.

[Specification, page 18, lines 4-7, emphasis added]

> ...peptide sequences containing transition state analog dipeptide isosteres, according to the invention, at the bond that is required to be hydrolyzed by the catalytic antibodies of the present invention **define a sequence that the catalytic antibody will hydrolyze in a native protein**.

[Specification, page 20, lines 17-22, emphasis added]

A skilled artisan would readily understand from the disclosure in the Specification that the reaction of interest is the cleavage or formation of an ester or peptide linkage. (See, Claims 45 and 48).

Appellants do not agree with the Examiner's assertion that the Specification is deficient under 35 U.S.C. § 112 and respectfully submit that the chemical reactions catalyzed according to the preferred embodiments of the instant invention are clearly defined in the Specification. However, to further clarify the claimed subject matter Appellants offer to amend claims 39 and 42 as follows (deletions are identified with square brackets and additions are underlined):

> Claim 39: A catalytic antibody which catalyzes [a chemical reaction of interest] cleavage or formation of an ester bond or peptide linkage and which is elicited...
>
> Claim 42: A method for producing antibodies which catalyzes [a chemical reaction of interest] cleavage or formation of an ester bond or peptide linkage and which are elicited...

The Examiner further asserts, "The specification teaches how to make the hapten but does not teach that any of the myriad possibilities of formula (I) will make antibodies that have catalytic

activity..." (Examiner's Answer, par. 10, bottom of page 3, emphasis in the original). Again this assertion does not support the Examiner's "written description" rejection.

In any event, Appellants remind the examiner that working examples are not a requirement for satisfying either the "written description" or "enablement" requirements of the first paragraph of 35 U.S.C. § 112 (See, MPEP Sections 2163 and 2164.02). Thus, the fact that the application does not contain working examples is irrelevant to a patentability determination under the "written description" requirement.

Appellants submit that an objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). As stated in *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. (See, MPEP 2163.01). The Appeal Brief elaborates on how the Specification demonstrates to a skilled artisan that the inventors were in possession of the instant invention at the time the application was filed. Therefore, there is no basis for the Examiner's continued rejection of the claims under the "written description" requirement of 35 USC § 112, first paragraph.

Appellants again note that it still appears from the Examiner's arguments and assertions that the Examiner is confusing the "written description" and the "enablement" prongs of 35 U.S.C. § 112, first paragraph. In any event, Appellants submit that the claims fully comply with both the "written description" and the "enablement" requirements of the first paragraph of 35 USC § 112 for the reasons

set forth above and in Appellant's Appeal Brief filed April 30, 2002 and therefore request that the rejection be reversed.

C. With respect to paragraph (11) ("*Response to Argument*") of the Examiner's Answer, the Examiner asserts that "the teachings on pages 75-81 [of the Specification] are general teachings as to possible catalytic cleavages and a possible method to detect these cleavages, but there is nothing in the cited passage that would indicate to one of ordinary skill in the art that applicant had possession of the claimed catalytic antibodies when the application was filed" (Examiner's Answer, par. 11, page 4, emphasis in the original).

Appellants remind the Examiner that possession may be shown in a variety of ways and actual reduction to practice is only one of the ways to satisfy the "written description" requirement. The term "possession" used in the "written description" does not require that Appellants have made and tested the claimed compounds. The term merely refers to the requirement that the Appellants had invented the claimed subject matter at the time of filing the application. Therefore, the detailed description in the Specification of the catalytic cleavage and a method to detect this cleavage, while termed "possible" by the Examiner, does not preclude a skilled artisan from determining that the Appellants were in the full possession of the claimed subject matter pursuant to the written description requirement.

Appellants urge that the Specification describes distinguishing identifying characteristics of the invention, such as chemical formulae of the haptens to elicit catalytic antibodies for catalyzed cleavage, sufficient to establish that the Appellants were in the full possession of the instant invention.

The MPEP clearly states:

> An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive

means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). **Possession may be shown in a variety of ways** including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such **as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention**. See, e.g., *Pfaff v. Wells Electronics, Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406; *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (**one must define a compound by "whatever characteristics sufficiently distinguish it"**).

[MPEP 2163, emphasis added]

The Examiner further alleges the instant case is similar to the case in *re Armbruster, 185 USPQ 152 (CCPA 1975)* and asserts that "… a catalytic antibody and a method of making it are disclosed 'within broad ranges' but no 'specific formulation' is described that would produce the catalytic antibody" (Examiner's Answer, par. 11, page 5). This case does not support the Examiner's contention of a "written description" requirement. The court in *In re Armbruster, 185 USPQ 152 (CCPA 1975)* discusses the "enablement" requirement of the 35 U.S.C. § 112, first paragraph, and not the "written description" requirement.

Moreover, contrary to the Examiner's suggestion, the currently pending claims are directed towards catalytic antibodies and methods of their production and use, wherein the catalytic antibodies are elicited by a class of haptens which contain a clearly defined transition-state analog – trigonal boronate defined by formula (I). Furthermore, the Specification provides the extensive disclosure of the claimed compounds and the detailed description of the various synthetic methods for preparing the claimed compounds (e.g., Specification, Example 3).

The Examiner further relies on *Fiers v. Revel 25 USPQ 1601 (Fed. Cir, 1993)* and alleges that "the instant specification merely states 'a wish to know the identity of any material with [the activity of

the catalytic antibody and is] not a proper written description' because appellant has not shown one of ordinary skill in the art that he knew at the time the application was filed which embodiments of the very broad range included within the scope of the hapten (formula (I)) would produce a catalytic antibody and which would not" (Examiner's Answer, par. 11, page 5, emphasis in the original). This case also does not support the Examiner's contention of a "written description" requirement. The quote cited by the Examiner from *Fiers v. Revel 25 USPQ 1601 (Fed. Cir, 1993)* relates to the court's discussion of the "enablement" requirement not the "written description" requirement.

Furthermore, Appellants urge that it is not proper to apply the "enablement" standards used for nucleic acids to the "written description" requirements for catalytic antibodies, which are defined by the hapten used in the methods of making these catalytic antibodies. The MPEP clearly states:

> For some biomolecules, examples of identifying characteristics include a sequence, structure, binding affinity, binding specificity, molecular weight, and length. **Although structural formulas provide a convenient method of demonstrating possession of specific molecules, other identifying characteristics or combinations of characteristics may demonstrate the requisite possession**. For example, unique cleavage by particular enzymes, isoelectric points of fragments, detailed restriction enzyme maps, **a comparison of enzymatic activities, or antibody cross-reactivity may be sufficient to show possession of the claimed invention** to one of skill in the art. See *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966 ("written description" requirement may be satisfied by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention").

[MPEP 2163, page 2100-161, emphasis added]

The Specification provides identifying characteristics such as binding specificity, which is determined by the hapten of formula (I), and enzymatic activity, which is determined by the transition-state analog engineered into the hapten of formula (I). Appellants submit that the described identifying characteristics are sufficient to show possession of the claimed invention.

Appellants maintain that as it was set forth in the Appeal Brief, this case is similar to *Reagents of the University of California v. Eli Lily*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), where the court stated:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus.

The Examiner further alleges, "it is maintained that the catalytic antibody is sufficiently unpredictable that without some guidance which hapten will produce antibodies that are catalytic and which will only produce antibodies that have no catalytic activity, the broad formula (I) is not adequate written description" (Examiner's Answer, par. 11, page 6, emphasis in the original). This unsupported assertion does not support a "written description" rejection.

As it was set forth above, the Examiner has admitted that the Specification provides sufficient guidance to make the haptens of formula (I) as defined in the instant invention. In addition, the Specification also provides guidance as to how to elicit an immune response and how to screen antibodies for catalytic activity using the haptens of formula (I). In fact, such antibody producing methods are well known in the art.

Moreover, the fact that some embodiments of the instant invention may be non-functional is immaterial to the "written description" requirement. That is, the fact a claim may include non-functional embodiments is not relevant in determining whether inventors had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by them pursuant to the first paragraph of 35 USC § 112. Again, the test for written description under 35 U.S.C. § 112, first paragraph, is whether the originally filed Specification reasonably conveys to a person having ordinary skill in the art that Appellants had possession of the subject matter later claimed. *In re*

Kaslow, 217 U.S.P.Q. 1089 (Fed. Cir. 1983). [See also, MPEP, Section 2163.02]. Appellants maintain that screening methods for antibodies having catalytic properties were readily available to a person of ordinary skill in the art at the time this application was filed. Therefore, a person of ordinary skill in the art would readily recognize that Appellants were in possession of the claimed invention at the time the application was filed.

Furthermore, Appellants urge that there is no basis for the Examiner's assertion that the art is unpredictable. In any event, the Examiner's unsupported assertion of unpredictability does not support a rejection based on the written description requirement of the first paragraph of 35 USC § 112.

The Examiner cites Gao et al. (Gao) to show the unpredictability of the art stating, "Only one particular hapten (3a) is shown to produce a catalytic antibody and that antibody will act on only one substrate (1a). The catalytic antibody will not cleave the diastereomer (1b) nor ester substrates (1c or 1d)" (Examiner's Answer, par. 11, page 6, emphasis in the original). Appellants urge that contrary to the Examiner's assertion that Gao supports the unpredictability of the art, the reference shows that an antibody can be produced by a hapten (3a) containing trigonal boronate and this catalytic antibody is highly specific. The antibody will not catalyze reaction of "promiscuous" substrates (1b-1d), but will catalyze the reaction of substrate 1a with high efficiency. The specificity of an antibody cannot be confused with unpredictability of the art. Moreover, the reference provides evidence that one of ordinary skill in the art can readily determine the specificity of an antibody without undue experimentation.

Furthermore, the Examiner dismisses the Nevinsky, et al. reference, as showing the state of the art in the year 2000.

Appellants submit that the review article by Nevinsky et al. provides information regarding the development of the art from the time preceding the instant application to the time following the instant

application. For example, none of the 23 references presented in the table on pages 1237-1239 of Nevinsky et al. was published subsequent to the filing date of the instant application. Accordingly, the Nevinsky reference provides evidence which is relevant to any question regarding enablement of the claimed subject matter.

Since the Examiner has specifically stated that " the instant rejection is not an enablement rejection" (Examiner's Answer, par. 11, page 7, emphasis in the original), the predictability of the art and the relevance of cited references need not be discussed further.

CONCLUSIONS

In view of the foregoing, Appellants urge that the currently pending claims of the instant application are fully supported by the original Specification in compliance with the "written description" requirement of 35 U.S.C. § 112, first paragraph. The reversal of the rejection of claims 36, 39, 42, 45 and 48 under 35 U.S.C. § 112, first paragraph, is earnestly solicited.

Respectfully submitted,

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